Trouble with trials

While developing the Annual Evidence Update on Acne Vulgaris from 25 randomized controlled trials (RCTs) from 2009, Ingram and colleagues discovered a high frequency of problems with the reporting and interpretation of the data. By highlighting the common problems in these studies, the authors hope not only to reduce bias for future results but also to improve patient welfare and influence the future of clinical acne trials. Interestingly, major problems of trial reporting were identified in 12 of these 25 RCTs; among the issues were a lack of statistical power, duplicate publication, testing of the wrong outcome, "salami publication," absent inferiority margins, reports of two independent studies as one, lack of true double-blinded trials, absent data, data fishing, impressive *P*-values, and inflated odds ratios. In the future, such problems can be circumvented through prospective trial registration and adherence to the CONSORT (Consolidated Standards of Reporting Trials) guidelines, which provide the gold standard for RCT reporting. (*Trials* 11:77, 2010)

The underlying relationship

The incidence of malignant melanoma has been rising in prosperous white populations. Earlier diagnosis and a consequent improvement in prognosis have been achieved. In addition, in the United States, a systematic proportional relationship between incidence rates for *in situ* melanoma and invasive melanoma across all ages has been observed. Lee examined the Statistics Epidemiology and End Results Program of the US National Cancer Institute data for *in situ* and invasive melanoma in white individuals from 1975 to 2004. The log incidence and log invasive rate for malignant melanoma were found to be critical characteristics of this disease. This relationship is independent of year, gender, or age and is sufficiently strong to exclude other factors such as diagnosis or historical change. Furthermore, these results probably stem from individual differences in melanoma rates and responses within populations. (*Dermatol Res Pract*, published online 28 June 2010; doi:10.1155/2010/839829)

Disappearing microneedles

The traditional intramuscular injection of influenza vaccine has been very successful; however, the necessary hypodermic needles cause needle phobia and biohazardous waste. Recently, Sullivan and colleagues reported the development of dissolving polyvinylpyrrolidone microneedle patches for influenza vaccination. The polymer microneedles dissolve in the skin within minutes and are eliminated by the body. These microneedles increase a vaccine's immunogenicity by targeting the antigen directly to the skin at a depth that maximizes interaction with the plethora of resident antigen-presenting cells. A robust humoral and cellular immune response was induced following use of this vaccination technique, which employs lyophilized antigen at a very low dose. In addition, a single vaccination conferred protective immunity against lethal viral challenge in mice. Although the immunological responses were similar between delivery via the microneedle patch and intramuscular injection, an enhanced recall immune response, increased numbers of antibody-secreting cells, and more efficient viral clearance were observed after administration with the microneedle patch. Thus, the dissolving microneedle patches appear to provide a safer, more immunogenic, and logistically better approach for the administration of influenza vaccine, allowing for the possibility of increased population coverage. (*Nat Med* 16:915–20, 2010)

At the root of hair loss

Alopecia areata (AA) is a common autoimmune disease that affects 5.3 million Americans and results in loss of hair triggered by the collapse of immune privilege. Because the underlying genetic basis of AA is unknown, Petukhova and colleagues performed a genome-wide association study with 1,054 AA cases and 3,278 controls using a combination of Illumina 610K and 550K arrays. This analysis identified 139 single-nucleotide polymorphisms (SNPs) that are significantly associated with AA, and these SNPs clustered into eight genomic regions that contained genes such as *CTLA4*, *IL-2/IL-21*, *HLA*, *ULBP* genes, and *IL-2RA*. Interestingly, this study implicated a new class of NKG2D ligands, the *ULBP* genes, in autoimmune disease. Indeed, functional studies demonstrated that the autoimmune destruction in AA may result, in part, from $CD8^+NKG2D^+$ cytotoxic T cells that are activated by the upregulation of ULBP3 in the hair follicle. This exciting result offers new insight into the underlying mechanism of AA and provides a novel target for the development of therapies. (*Nature* 466:113–7, 2010)

Commonalities in Turkey and Japan

In two complementary studies, Remmers and Mizuki, along with their respective colleagues, performed genome-wide association studies to identify the genetic variants that underlie Behçet's disease, a genetically complex disease of unknown origin that is prevalent in Middle Eastern countries as well as in Japan. Remmers and colleagues examined 311,459 single-nucleotide polymorphisms (SNPs) from 1,215 Behçet's cases and 1,278 healthy controls from Turkey, and Mizuki and colleagues examined 320,438 SNPs from 611 Behçet's cases and 737 controls from Japan. Both studies confirmed the known association between *HLA-B*51* and this disease. After a data exchange between the groups to facilitate data-set validation, *IL10* and *IL23R-IL2RB2*, which are critical for the immune response, were identified as new susceptibility loci for Behçet's disease in both populations. (*Nat Genet* 420:698–702, 2010; *Nat Genet* 420:703–6, 2010)

Journal of Investigative Dermatology (2010) **130,** 2533. doi:10.1038/jid.2010.286